DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-845/S-001

INO Therapeutics, Inc.
Attention: Mr. Jared S. Rhines
54 Old Highway 22
Clinton, NJ 08809

Dear Mr. Rhines:

Please refer to your supplemental new drug application dated December 20, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for INOmax (nitric oxide) 100 ppm and 800 ppm for Inhalation.

We acknowledge receipt of your submission dated March 19, 2001. Your submission of March 19, 2001 constituted a complete response to our February 20, 2001 action letter.

This supplement provides for final printed labeling wherein the following paragraph has been added the Clinical Trials section:

> In a randomized, double-blind, parallel, multicenter study, 385 patients with adult respiratory distress syndrome (ARDS) associated with pneumonia (46%), surgery (33%), multiple trauma (26%), aspiration (23%), pulmonary contusion (18%), and other causes, with PaO_2 <250 mmHg despite optimal oxygenation and ventilation, received placebo (N=193) or INOmax (N=192) 5 ppm for 4 hours to 28 days or until weaned because of improvements in oxygenation. Despite acute improvements in oxygenation, there was no effect of INOmax on the primary end point of days alive and off ventilator support. These results were consistent with outcome data from a smaller dose ranging study of nitric oxide(1.25 to 80 ppm). INOmax is not indicated for use in ARDS.

Please change PaO_2 <250 mmHg to PaO_2/FiO_2 <250 mmHg in the first sentence.

In addition, the second sentence of the DESCRIPTION section has been changed from:

> INOmax is a gaseous blend of nitric oxide (0.8%) and nitrogen (99.2%).
>
> To:
>
> INOmax is a gaseous blend of nitric oxide and nitrogen (0.08% and 99.92%, respectively for 800 ppm; 0.01% and 99.99%, respectively for 100 ppm).

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the final printed labeling included in your March 19, 2001 submission. Accordingly, the supplemental application is approved effective on the date of this letter.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Ms. Zelda McDonald
Regulatory Health Project Manager
(301) 594-5333.

Sincerely,

{See appended electronic signature page}

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research